A Mechanism for the Association of Amino Acids with their Codons and the Origin of the Genetic Code

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The genetic code has certain regularities that have resisted mechanistic interpretation. These include strong correlations between the first base of codons and the precursor from which the encoded amino acid is synthesized, and between the second base of codons and the hydrophobicity of the encoded amino acid. These regularities are even more striking in a projection of the modern code onto a simpler code consisting of doublet codons encoding a set of simple amino acids. These regularities can be explained if, before the emergence of macromolecules, simple amino acids were synthesized in covalent complexes of dinucleotides with α–keto acids originating from the reductive tricarboxylic acid cycle or reductive acetate pathway. The bases and phosphates of the dinucleotide are proposed to have enhanced the rates of synthetic reactions leading to amino acids in a small-molecule reaction network that preceded the RNA translation apparatus, but created an association between amino acids and the first two bases of their codons that was retained when translation emerged later in evolution. This is a significant departure from previous theories attempting to explain the regularities in the genetic code.

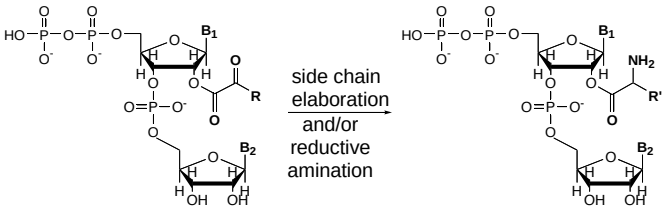

Figure 1. Model for synthesis of amino acids from α-keto acid precursors covalently attached to dinucleotides. The dinucleotide that is capable of catalyzing synthesis of a

particular amino acid is proposed to contain the first two bases of the codon specifying that amino acid.